IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of

Patrick RAMBAUD Conf. 1794

Application No. 10/687,636 Group 1631

Filed October 20, 2003 Examiner P. Whaley

METHOD AND SYSTEM FOR MANAGING BATCHES OF IMMUNOCOMPETENT CELLS COLLECTED FROM HUMAN OR ANIMAL SUBJECTS FOR DEFERRED USE, AND RELATED THERAPY METHODS

APPEAL BRIEF

MAY IT PLEASE YOUR HONORS:

(i) Real Party in Interest

The real party in interest in this appeal is the assignee, Sankhia International Inc. of Tortola, British Virgin Islands.

(ii) Related Appeals and Interferences

None.

(iii) Status of Claims

Claims 1-32 and 35 have been cancelled. Claims 33-34 and 36-54 are pending and rejected. Claims 33-34 and 36-54 were rejected by the final Official Action mailed

August 10, 2011 (the "Official Action"). The final rejection of claims 33-34 and 36-54 is being appealed.

(iv) Status of Amendments

No amendment has been filed subsequent to the Official Action finally rejecting claims 33-34 and 36-54.

(v) Summary of Claimed Subject Matter

Claims 33 and 36 are independent.

Claim 33 is directed to a system for managing batches of immunocompetent cells collected from human or animal subjects for their deferred use.

Claim 36 is a method for managing batches of immunocompetent cells collected from human or animal subjects for deferred use.

Claim 33

Claim 33 recites a system for managing batches of immunocompetent cells collected from human or animal subjects for their deferred use (published application paragraph [0002], [0005] specification page 1, lines 8-13, 22-28; Figures 1-2 generally).

The system comprises for each of said human or animal subjects:

- a storage device for conditioning and preserving batches of immunocompetent cells successively collected, into one or more storage centers ([0020]/[0047], specification page 4, lines 1-2; Figure 1, storage sites 1, i, n)

- a personal library processor for constituting from said collected batches a personal library of immunocompetent cells, said personal library cumulating a

sum of immunity information stored in the membranes of collected immunocompetent cells ([0021]/[0048], specification page 4, lines 3-6; Figure 1, Personal library),

- a collection device for collecting, during successive collections of batches, information that is characteristic of said human or animal subject's status of health and/or psychological status, before or during immunocompetent cells collection, said status characterizing information being obtained by processing measurements made on samples of blood and/or fluid and secretions and/or hair collected on said human or animal subject ([0022]/[0049], specification page 4, lines 7-13; Figure 1 Collection section including blood collection, separation, cell identification, etc.),

- a status-characterizing information device processing said status-characterizing information to determine said subject's identity data ([0023]/[0050], specification page 4, lines 14-15), said identity data including immunity-related data, historical and clinical data on previous diseases, treatments and therapeutic protocols experienced by said subject, said status-characterizing information device comprising an expert system wherein said status-characterizing information

corresponding to said subject are entered in the form of biological items to which a set of rules stored in a knowledge base is applied, implementing into said expert system a process for determining a deferred-use protocol, said deferred-use protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells previously collected from said subject ([0035], [0078], [0085], [0091-0093], [0095], [0099], specification page 14, line 24 - page 16, line 30; Figure 1, Expert System block with Rules; Figure 2 generally),

- a cell management database processor for storing said subject's identity data successively determined into a cell management database ([0024]/[0051], specification page 4, lines 16-17; Figures 1-2, data base cell mangagement),

- an identification device for performing identification of the personal batches of cells and a consulting device for consulting said cell management database ([0025]/[0052], specification page 4, lines 18-22; Figure 1 within Deferrred Use, the Cell Batch identification block), and

- a processor for processing said successively collected subject's identity data to determine parameters of a deferred-use protocol for said identified batches of

immunocompetent cells ([0026]/[0051], specification page 4, lines 23-25; Figure 2, Deferred-Use protocol block), said processor configured for upon prescription of a re-use process of immunocompetent cells for said subject:

- determining parameters of said deferred-use protocol, using data stored in said database, said determined parameters including optimized proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, using the subject's immunity data stored in said database ([0054]-[0055], specification page 9, lines 4-10; Figure 2, data base, Deferred-Use protocol block), and

- determining said selected immunocompetent cells for extraction from said personal cell library ([0096], specification page 15, lines 14-20; Figure 2, personal cell library, cells collection blocks).

Claim 36

Claim 36 is directed to the method embodiment, i.e., a method for managing batches of immunocompetent cells collected from human or animal subjects for deferred use (published application paragraph [0002], [0005] specification page 1, lines 8-13, 22-28; Figures 1-2 generally).

The method includes:

plural successive cell collections stages of collecting immunocompetent cells collected from a human or animal subject for deferred use and storing the collected cells, in a storage device for conditioning and preserving the collected cells, into one or more storage centers ([0020]/[0047], specification page 4, lines 1-2; Figure 1, storage sites 1, i, n);

constituting for said subject, a personal cell library from the successively collected cells and a personal database, stored within a physical medium accessible by a computer system ([0021]/[0048], specification page 4, lines 3-6; Figure 1, Personal library), containing:

data resulting from successive status characterization stages effected before or during each cell collection stage, said data comprising information on said subject's physiologic identity and state of

health([0022]/[0049], specification page 4, lines 7-13; Figure 1 Collection section including blood collection, separation, cell identification, etc.), and

subject's identity data ([0023]/[0050], specification page 4, lines 14-15) generated by use of an expert system executed within the computer system and wherein said status-characterizing information corresponding to said subject are entered in the form of biological items to which a set of rules stored in a knowledge base is applied ([0035], [0078], [0085], [0091-0093], [0095], [0099], specification page 19, line 24 - page 16, line 30; Figure 1, Expert System block with Rules; Figure 2 generally),

implementing into said expert system a process for determining a deferred-use protocol, said deferred-use protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells previously collected from said subject ([0035], [0078], [0085], [0091-0093], [0095], [0099], specification page 19, line 24 - page 16, line 30; Figure 1, Expert System block with Rules; Figure 2 generally),

upon prescription of a re-use process of immunocompetent cells for said subject:

- determining parameters of said deferred-use protocol, using data stored in said database, said determined parameters including optimal proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, using subject's immunity data stored in said database([0054]-[0055], specification page 9, lines 4-10; Figure 2, data base, Deferred-Use protocol block),

- extracting said selected immunocompetent cells from said personal cell library ([0096], specification page 15, lines 14-20; Figure 2, personal cell library, cells collection blocks), and

- processing said extracted immunocompetent cells according to said deferred-use protocol, in view or re-using said processed cells into said subject ([0099], specification page 16, lines 2-13, Figure 2,, re-use process block.

Additionally, as to determining parameters that include "optimized proportions" and determining optimized parameters using "immunity data", from the published application there is disclosed:

[0036] The process of the status-characterizing information is arranged for determining respective optimal proportions of different immunocompetent cells in view of their deferred use, and, for example, can provide with a determination of an optimal ratio between lymphocytes T4 and T8 in view of their deferred use.

[0089] Said batch is the processed to room temperature and immunocompetent cells are put in culture and/or submitted to an ex-vivo process. Parameters of a protocol of re-use are determined by requesting identity data from the cell management database and processing said identity data to determine for example optimal ratio between lymphocytes T4 and T8 for re-injection. In view of a deferred-use therapeutic process for a patient, the cell treatment entity is therefore provided with one or several identified batches of cells from said patient and with determined re-use or deferred-use protocol parameters.

[0096] When a re-use process of immunocompetent cells is prescribed for a human or animal subject, a protocol of deferred-use is determined using data stored in

the database with, for example, optimal proportions between each type of cells. Selected immunocompetent cells are then extracted from the personal cell library and, if necessary, processed ex-vivo. When these immunocompetent cells are ready for use, a re-use process according to the determined personal protocol is effected at instant Tu.

[0099] It has to be noted that a management system according to the invention can be entirely automated, from the collection of information characteristic of the physical and/or biological status of a subject, through the preservation and storage of immunocompetent cells, up to the determination of protocols for deferred-use of said immunocompetent cells. The protocol determination process can be advantageously implemented in an expert system processing past experimental and clinical data related to deferred-use cumulated practice. For example, a deferred-use protocol may comprise as a way of non-limitative example, an optimal time schedule indicating the proposed dates for deferred use depending on collected personal parameters and therapeutic indications for re-use, and biological and technical indications required for cell processing before re-use.

As to determining optimized parameters using "immunity data", see the following:

Abstract: A method for …, said personal library cumulating a sum of immunity information stored in the collected immunocompetent cells, This method further comprises: gathering information characteristic of the status of said human or animal subject, effected before or during the immunocompetent cells collection, and processing said characteristic information for determining parameters of a deferred-use protocol for immunocompetent cells from said human or animal subject's personal library.

[0007] … These immunocompetent cells constitute in fact a library, in particular a lymphocyte library, which is enhanced during life, when the body meets foreign organisms, during viral, parasitic or bacterial infections. By means of this "immunity library", the body can minimize the impact of the infections during life. The action mechanism of the immune system is already known. Information are stored in the walls of lymphocytes, as illustrated by the transfer factor and reported by numerous publications. This mechanism also contributes to the defense against malignant cells.

[0021] constituting and enhancing from collected batches a personal library of immunocompetent cells, said personal library cumulating a sum of immunity information stored in the walls of the collected immunocompetent cells,

[0029] By means of the successively collected batches of immunocompetent cells from a person, a personal library is therefore constituted for said person. This personal library, which gathers immunity information stored in the walls of the collected immunocompetent cells, can be accessed on demand, when required for a therapeutic protocol, in order to provide with pertinent immunity concerning the patient.

[0031] The status-characterizing information is processed to determine a subject's identity data, for example by extracting from said status-characterizing information relevant data on personal immunity history and data. The subject's identity data may include immunity-related data, historical and clinical data on previous diseases, treatments and therapeutic protocols experienced by said subject.

[0035] The status-characterizing information and the immunity information stored in the immunocompetent cells of said human or animal subjects are advantageously entered into an expert system used for determining parameters for deferred-use protocols. This expert system can be arranged for providing an interpretation of said status-characterizing information and said immunity information with respect to a particular gene.

The specification discloses that the “deferred-use protocols” concern a future use of cells in a person and indicates how and in which conditions (concerning the cells and the person) to introduce the cells in the body of a person whereas a medical treatment recommendation is directed to a person and indicates how to use this medicine.

In the case of the deferred use protocol of cells, the state of the person at the moment of the re-use is not the only parameter. The deferred use protocol also concerns the re-used cells, the state of the person at the moment the cells have been taken, potential treatment of the cells before injection, etc. All these parameters are variable and differentiate the feature “deferred-use protocol” from the feature “medical treatment recommendation”.

See paragraph [0032]: The deferred-use protocol comprises, as a way of non limitative example, a plurality of steps or sequences for retrieving and reconditioning previously stored and preserved batches of immunocompetent cells in view of using said cells for re-injection, and steps for processing the subject's identity data in order to determine for example what type of immunocompetent cells must or can be used with regards to the object of said deferred-use for a given patient, and how and when such selected immunocompetent cells have to be injected in

relation with the patient's health status. This protocol can implement deferred-use parameters such as qualitative and quantitative data on the reconditioned immunocompetent cells, and physiological parameters related to the subject's health status in view of cell auto-use. Also see at least application paragraph [0089], [0096].

(vi) **Grounds of Rejection to be Reviewed on Appeal**

I. A first ground of rejection presented for review on appeal is whether claim 45 was properly rejected as unpatentable 35 USC § 112, 1st Paragraph. Claim 45 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, in that the Examiner states that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention (Official Action page 2, last paragraph).

II. A second ground of rejection presented for review on appeal is whether claims 33, 34, and 36-54 were properly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention (paragraphs spanning pages 3-4 of the Official Action).

III. A third ground of rejection presented for review on appeal is whether claims 33, 36, 37, 38, 39, and 43 were properly rejected under 35 U.S.C. 103(a) as being unpatentable over Lefesvre et al. (WO/1999/053030; p.1-5; English translation version), in view of Winkel (Clinical

Chemistry, 1989, 35/8, p.1595-1600), and in view of Adrion et al. (US 5,023,785) (Official Action page 6, first paragraph).

IV. A fourth ground of rejection presented for review on appeal is whether Claims 34 and 40 were properly rejection under 35 U.S.C. 103(a) over Lefesvre et al. in view of Winkel, and Adrion et al., as applied to claims 33, 36, 37, 38, 39, and 43, and further in view of Zanin et al. (WO/1997/045056) and Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137) (Official Action page 11, last paragraph).

V. A fifth ground of rejection presented for review on appeal is whether claim 42 was properly rejected under 35 U.S.C. 103(a) over Lefesvre et al. in view of Winkel, Adrion et al., Zanin et al., Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137), as applied to claims 33, 34, 36, 37, 38, 39, 40, and 43, and further in view of Tomoyasu (Applied And Environmental Microbiology, Jan. 1998, p. 376-382) (Official Action page 13, first full paragraph).

VI. A sixth ground of rejection presented for review on appeal is whether claims 41 and 44-54 were properly rejected under 35 U.S.C. 103(a) over Lefesvre et al., Winkel, Adrion et al. Zanin et al., ad Cha et al., Tomoyasu, as applied to claims 33, 34, 36, 37, 38, 39, 40-43, and further in view of Privitera et al. (US 4,826,760)

and Barocci et al. (Transpl. Int., 1993, 6:29-33) (Official Action page 14, first full paragraph).

(vii) Arguments

Arguments Concerning the First Ground of Rejection

The first ground of rejection presented for review is whether claim 45 was properly rejected as unpatentable 35 USC § 112, 1st Paragraph.

Claim 45 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, in that the Examiner states that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention (Official Action page 2, last paragraph).

Claim 45 recites "wherein the autologous vaccine is a flu vaccine with cytotoxic activity." The rejection states that no basis has been pointed to for these new limitations and no support has been found in the specification.

Published application paragraph [0009] discloses “Moreover, errors are introduced with time and the immunity becomes usually less efficient with years. Because of this degradation, infections as flu are far more dangerous for aged persons. Furthermore, it would be particularly

interesting to preserve information acquired along a whole life."

Published application paragraph [0040] discloses that "Another promising way of implementation for the management method according to the invention relates to therapy protocols including an ex vivo processing between lymphocytes and a vaccine before re-injection. No production of antibodies has been observed."

Published application paragraphs [0037] and [0058] disclose that "When the method according to the invention is implemented in a therapeutic protocol including re-injecting lymphocytes on a human or animal subject, the previously collected and preserved immunocompetent cells can be submitted to an ex-vivo process before being re-injected. The method according to the invention can also be implemented in a therapeutic protocol including re-injecting lymphocytes T with a specific cytotoxic activity after ex-vivo expansion, or in a gene therapy protocol." and "The therapy protocol can include re-injecting lymphocytes T with a specific cytotoxic activity after ex-vivo expansion."

Original claim 7 recited "The method according to claim 6, implemented in a therapeutic protocol including re-injecting lymphocytes T with a specific cytotoxic activity after ex-vivo expansion."

Although the original specification did not include the express phrase of an autologous vaccine being a flu vaccine with cytotoxic activity, Appellant respectfully submits that one of skill, having read the specification would understand that at the time the application was filed, Appellant had possession of the claimed invention.

Therefore, this rejection is improper.

Arguments Concerning the Second Ground of Rejection

The second ground of rejection presented for review is whether claims 33, 34, and 36-54 were properly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention (paragraphs spanning pages 3-4 of the Official Action).

Claim 33

The rejection states that claim 33, in lines 30-35, recites "implementing into said expert system a process for determining a deferred use protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells … from said subject", which appears to be a method step and "as the claimed invention is directed to a device, the recitation of an apparent method step renders the claim confusing."

Appellant disagrees. Appellant notes that there is no rejection, as to the recitation, under 35 U.S.C. 112, first paragraph, and no statement that the language itself is indefinite.

The objected-to passage does include functional language. However, functional language is not *per se* impermissible.

In an article, apparatus, or system claim, the issue is what "is" the inventive article, apparatus, or system and how is the inventive article, apparatus, or system structurally different from the prior art (i.e., is it novel and non-obvious?).

The MPEP acknowledges that functional language functional language, *per se*, is not impermissible. See http://www.uspto.gov/web/offices/pac/mpep/documents/2100_2114.htm. Further, see MPEP 2173.05(g) Functional Limitations:

http://www.uspto.gov/web/offices/pac/mpep/documents/2100_2173_05_g.htm

There is nothing inherently wrong with defining some part of an invention in functional terms. A functional limitation must be evaluated and considered for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used to define a particular capability or purpose that is served by the recited element. For example, the term "operatively connected" is a general descriptive claim term frequently used in patent drafting to reflect a

functional relationship between claimed components, that is, the term "means the claimed components must be connected in a way to perform a designated function."

Further, the MPEP sections indicate that it was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought; that in a claim that was directed to a kit of component parts capable of being assembled, the Court held that limitations such as "members adapted to be positioned" and "portions … being resiliently dilatable whereby said housing may be slidably positioned" serve to precisely define present structural attributes of interrelated component parts of the claimed assembly.

Appellant respectfully submits the “functional language” identified by the rejection is not in itself indefinite and must be given patentable weight, as such language requires the claimed element to necessarily have certain characteristics.

Therefore, this rejection is improper.

Claims 33 and 36

The rejection states that claims 33 and 36, in the last 8 lines, recite "determining parameters ... , using data stored in said database, said determined parameters including optimized proportions … for better tolerance … and greater reaction speed, using the subject's immunity data stored in the database." The rejection states that “the use of two separate "using" phrases makes it unclear what data is used for determining parameters. For example, one interpretation of the claims is that parameters are determined using ANY of the data stored in said database. However, a second interpretation is that parameters are determined using the immunity data stored in the database. Which is it? Clarification is requested.”

The complete recitation is:

- determining parameters of said deferred-use protocol, using data stored in said database, said determined parameters including optimized proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, using the subject’s immunity data stored in said database,

Appellant believes the recitation is definite, i.e.,

determining parameters of said deferred-use protocol, **[the parameters determination made]** using data stored in said database,

said determined parameters including optimized proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, **[the optimized proportions determined]** using the subject's immunity data stored in said database.

Further, one skilled in the art, having read and understood the specification would recognize that the invention included determining parameters that include "optimized proportions" and determining optimized parameters using "the subject's immunity data".

As to "optimized proportions", one of skill would understand that this relates to optimal proportions and optimal ratio. From the published application please see the following paragraphs:

[0036] The process of the status-characterizing information is arranged for determining respective optimal proportions of different immunocompetent cells in view of their deferred use, and, for example, can provide with a

determination of an optimal ratio between lymphocytes T4 and T8 in view of their deferred use.

[0089] Said batch is the processed to room temperature and immunocompetent cells are put in culture and/or submitted to an ex-vivo process. Parameters of a protocol of re-use are determined by requesting identity data from the cell management database and processing said identity data to determine for example optimal ratio between lymphocytes T4 and T8 for re-injection. In view of a deferred-use therapeutic process for a patient, the cell treatment entity is therefore provided with one or several identified batches of cells from said patient and with determined re-use or deferred-use protocol parameters.

[0096] When a re-use process of immunocompetent cells is prescribed for a human or animal subject, a protocol of deferred-use is determined using data stored in the database with, for example, optimal proportions between each type of cells. Selected immunocompetent cells are then extracted from the personal cell library and, if necessary, processed ex-vivo. When these immunocompetent cells are ready for use, a re-use process according to the determined personal protocol is effected at instant Tu.

[0099] It has to be noted that a management system according to the invention can be entirely automated, from

the collection of information characteristic of the physical and/or biological status of a subject, through the preservation and storage of immunocompetent cells, up to the determination of protocols for deferred-use of said immunocompetent cells. The protocol determination process can be advantageously implemented in an expert system processing past experimental and clinical data related to deferred-use cumulated practice. For example, a deferred-use protocol may comprise as a way of non-limitative example, an optimal time schedule indicating the proposed dates for deferred use depending on collected personal parameters and therapeutic indications for re-use, and biological and technical indications required for cell processing before re-use.

As to determining optimized parameters using "immunity data", see the following:

Abstract A method for …, said personal library cumulating a sum of immunity information stored in the collected immunocompetent cells, This method further comprises: gathering information characteristic of the status of said human or animal subject, effected before or during the immunocompetent cells collection, and processing said characteristic information for determining parameters

of a deferred-use protocol for immunocompetent cells from said human or animal subject's personal library.

[0007] … These immunocompetent cells constitute in fact a library, in particular a lymphocyte library, which is enhanced during life, when the body meets foreign organisms, during viral, parasitic or bacterial infections. By means of this "immunity library", the body can minimize the impact of the infections during life. The action mechanism of the immune system is already known. Information are stored in the walls of lymphocytes, as illustrated by the transfer factor and reported by numerous publications. This mechanism also contributes to the defense against malignant cells.

[0021] constituting and enhancing from collected batches a personal library of immunocompetent cells, said personal library cumulating a sum of immunity information stored in the walls of the collected immunocompetent cells,

[0029] By means of the successively collected batches of immunocompetent cells from a person, a personal library is therefore constituted for said person. This personal library, which gathers immunity information stored in the walls of the collected immunocompetent cells, can be accessed on demand, when required for a therapeutic protocol, in order to provide with pertinent immunity concerning the patient.

[0031] The status-characterizing information is processed to determine a subject's identity data, for example by extracting from said status-characterizing information relevant data on personal immunity history and data. The subject's identity data may include immunity-related data, historical and clinical data on previous diseases, treatments and therapeutic protocols experienced by said subject.

[0035] The status-characterizing information and the immunity information stored in the immunocompetent cells of said human or animal subjects are advantageously entered into an expert system used for determining parameters for deferred-use protocols. This expert system can be arranged for providing an interpretation of said status-characterizing information and said immunity information with respect to a particular gene.

The above are examples that show, when read in light of the specification the recitation of "determining parameters …, using data stored in said database, said determined parameters including optimized proportions … for better tolerance … and greater reaction speed, using the subject's immunity data stored in the database" is definite.

Since the recitations are not indefinite, the rejection is improper.

Claim 41

The rejection states that amended claim 41 recites "checking annihilating antibodies .... "; and that it is unclear whether this phrase is intended to be a step for "checking" annihilating antibodies or is a step for "annihilating" antibodies, and that if the former is intended, it is unclear what is being "checked" for; e.g. the presence of antibodies or something else.

Claim 41 recites "…further comprising a step for checking annihilating antibodies in the batches of immunocompetent cells before any re-use of a batch."

Although the Examiner is allowed to interpret that claim recitations broadly, the Examiner must not interpret the claim recitation inconsistent with the specification.

MPEP § 2111 for guidance in giving the pending claims their broadest reasonable interpretation consistent with the specification. The MPEP § 2111 guidance does not authorize that the claim terms can take on any conceivable meaning the Examiner may create. The Examiner is limited such that the broadest reasonable interpretation of the claims are consistent with the interpretation that those skilled in the art would reach. In re Cortright, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999).

Claims 16-17, as presented for original examination, recited "before the step for cryo-preserving a batch of immunocompetent cells, a step of cryogenizing said batch in view of annihilating antibodies present within said batch." and "before any re-use of a batch of immunocompetent cells previously collected, a step for checking the annihilation of the antibodies within said batch."

Paragraph [0044] discloses "The management method according to the invention can further comprise, before the step of cryo-preservation of a batch of immunocompetent cells, an initial step for cryogenizing said batch arranged for causing the antibodies initially present in said batch to be annihilated. A step for checking the annihilation of other antibodies within the batch of immunocompetent cells can also be provided."

Further, paragraph [0082] discloses that "The deferred use of lymphocytes can raise problems if antibodies are preserved because, along the time, the concerned subject or patient may be submitted to a reaction against his or its own antibodies and to a reject of said antibodies. An initial step of cryogenization can be provided in order to annihilate antibodies within a batch of immunocompetent cells. Before reusing this batch of cells, a step for checking the effective annihilation of said antibodies is

provided. This checking step can implement known techniques for testing antibodies in batches of cells that have been previously cryo-preserved."

Appellant respectfully submits that, when "checking" and "annihilating antibodies" are interpreted consistent with the specification, the claim language is definite.

Therefore, the rejection is improper.

Arguments Concerning the Third Ground of Rejection

III. A third ground of rejection presented for review is whether claims 33, 36, 37, 38, 39, and 43 were properly rejected under 35 U.S.C. 103(a) as being unpatentable over Lefesvre et al. (WO/1999/053030; p.1-5; English translation version), in view of Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600), and in view of Adrion et al. (US 5,023,785) (Official Action page 6, first paragraph).

Appellant notes that the Examiner has different interpretations of Lefesvre in two different Official Actions. In the Official Action of 11/12/2010 (page 10) the Examiner clearly states that "Lefesvre doesn't teach an expert system that determines deferred-use protocol comprising biological and technical indications required for cell processing" whereas in the Official Action of 08/10/2011 (page 8) the Examiner states "Lefesvre doesn't specifically teach implementing deferred use protocols comprising biological and technical indications required for cell processing. However Lefesvre suggests this limitation".

In addition to the above, the Examiner recognizes (page 10 of the Official Action) that Lefesvre doesn't teach:

i) an expert system that applies a set of rules stored in a knowledge base; or

ii) parameters of deferred-use protocol that include optimal proportions of various selected cell types using the subject's immunity data.

To this extent, the Examiner is correct.

Winkel

The rejection states that Winkel discloses an expert system using rules for producing diagnostic results and treatment recommendations. (page 10 of Official Action). From there, the Examiner states that "it would have been obvious to someone of the ordinary skill in the art to modify the cellular re-use processing center of Lefesvre to include an expert system that applies a set of rules stored in a knowledge system".

Appellant respectfully points out that no objective evidence supports this conclusion, and therefore there is no factual/legal support for a finding of obviousness.

Winkel teaches several expert systems applied to clinical data.

Some of the expert systems disclosed in Winkel provide diagnostic results and treatment recommendations.

At page 1597, col. 2, Winkel discloses a table listing the most known expert systems emphasizing the use of laboratory data. However, none of the expert systems listed in this table is used in the domain of the reuse of cells, or the processing of parameters of a cell re-use protocol.

Moreover, the Examiner states that it would have been obvious "to include an expert system that applies a set of rules stored in a knowledge system".

However, the Examiner doesn't address: which set of rules stored in which knowledge system?

Indeed, none of the rules used in any of the expert systems described in Winkel is applicable to cell re-use protocol determination.

So, when including an expert system in a re-use processing center in order to determine cell re-use protocol parameters, a person having ordinary skills in the art has to define the set of rules which are not taught in Winkel. This is not an ordinary operation and is not obvious for an ordinary skilled person. Furthermore, the Examiner has not shown otherwise.

Moreover, Winkel repeatedly states that the adaptation of an expert system designed for a given domain

for use in a different domain is very difficult and can only be done if the requirements imposed by the problem are understood (see p.1597, col. 2 §3, p. 1598 col. 1 §2 §3 "the appropriate tool can be chosen only after requirements imposed by the problem are understood").

Finally, Winkel states as a conclusion that "the development of transparent systems ... that may be transferred between technical and medical environments and easily updated and modified by the end user represents a real challenge"(p.1599, col. 2, §2).

This sentence means that transferring an expert system of Winkel designed for the environment of treatment recommendations to cell reuse environment "represents a real challenge". This is objective evidence that the adaptation of the expert systems of Winkel for use in the domain of the reuse of cells is not obvious.

Adrion

Adrion teaches an expert systems outputting diagnostic information of a patient. In claim 4, Adrion discloses the name of the parameters taken into account in the diagnostic. The rejection states that Adrion teaches optimized parameters comprising the cell ratio amounts based on claim 1 and claim 4 (see Official Action page 10, lines 12-16).

Appellant respectfully disagrees as the Examiner has misinterpreted Adrion.

Adrion teaches an expert system outputting diagnostic information of a patient in the domain of hematology. However, the apparatus disclosed in Adrion comprises data processing means for "evaluating blood derived parametric values" and "means for "ascertaining clinically interval combination".

Adrion doesn't determine optimal proportions of cell types, but only combination of intervals. In Adrion claim 4, the expression "Iymphocyte/monocyte count" doesn't mean the ratio of lymphocyte/monocyte. Rather, the expression "lymphocyte/monocyte count" means "lymphocyte or monocyte count".

This interpretation is confirmed in Adrion claim 5 where it is stated that the " ... Iymphocyte/monocyte count ... is expressed in xl09/L". Indeed, if it was the ratio the count wouldn't be expressed in "/L" and wouldn't have any measurement unit.

At least for these reasons, Adrion doesn't disclose "determining parameters of deferred-use protocol including optimal proportions of various selected cell types using the subject's immunity data".

Thus, Adrion also doesn't disclose feature ii) parameters of deferred-use protocol that include optimal proportions of various selected cell types using the subject's immunity data.

Conclusions

From the above, it is shown that:

it is not obvious to include the expert system of Winkel in the cell processing center of Lefesvre, in order to reach to an expert system that applies a set of rules stored in a knowledge base in order to determine a cell re-use protocol; and

Adrion also doesn't teach feature ii) of parameters of deferred-use protocol that include optimal proportions of various selected cell types using the subject's immunity data.

Moreover, the above further shows that there is objective evidence in Winkel that the transfer of an expert system designed for a given domain to a different domain is not obvious for a person having ordinary skills in the art and rather represents a real challenge.

Accordingly, Appellant respectfully submits that neither independent claim 33 nor claim 36 is rendered obvious by Lefesvre in view of Winkel and Adrion.

The Declaration of Professor Dominique CHARRON provides further evidence of the claims being non-obvious.

In the Official Action's Response to Declaration section, the Examiner urges that Appellant's arguments, filed 05/12/2011, on page 24, that it would not have been obvious to one of ordinary skill in the art to combine the above references in view of the Declaration filed 05/12/2011 by Professor Dominique Charron, under 37 CFR 1.132, are insufficient to overcome the rejections of record under 35 U.S.C. 103(a).

Appellant again disagrees.

The Examiner states that Declaration does not refer to any of individual claims of the instant application. Appellant does not see how this is relevant when the Declaration as a whole is considered.

However, the Declaration itself is objective evidence of non-obviousness of the claimed subject matter, specifically the features for which the Declaration has been offered.

The Examiner states that the Declaration asserts that it was not obvious to determine and define parameters for deferred uses for stored immune-competent cells of a healthy individual because: (1) parameters to define or trigger a re-infusion of immuno-competent cells were not

available, and (2) parameters "supporting the need for storage" (e.g. longitudinal parameters) were known as medical parameters but were not linked to information required for stored cells of healthy patients.

With regards to (1), the instant claims do not recite "parameters to define or trigger a re-infusion of immuno-competent cells", but instead recites a step of determining parameters of a deferred-use protocol (see claim 33).

Appellant respectfully points out that the Examiner is not considering what the Declaration actually presents, and rather is requiring that there be a one-to-one mapping of the Declaration to the claims.

The correct issue is whether the Declaration is probative to the question of the obviousness of the claimed invention, taking into consideration the state of the prior art and the points raised in the Declaration.

The Examiner does not dispute Professor Charron that parameters, e.g. longitudinal immune data of healthy patients, were known as medical parameters but were not linked to information required for stored cells of healthy patients.

The Examiner has failed to give these statements any consideration in evaluating whether the claimed invention is obvious.

The Declaration does provide support that the invention, as to the subject matter discussed in the Declaration, is non-obvious.

For the above reasons, Appellant respectfully submits that the rejection of claims 33 and 36 is therefore improper.

Arguments Concerning the Fourth Ground of Rejection

The fourth ground of rejection presented for review is whether Claims 34 and 40 were properly rejection under 35 U.S.C. 103(a) over Lefesvre et al. in view of Winkel, and Adrion et al., as applied to claims 33, 36, 37, 38, 39, and 43, and further in view of Zanin et al. (WO/1997/045056) and Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137) (Official Action page 11, last paragraph).

These claims are allowable at least for depending from an allowable claim.

Arguments Concerning the Fifth Ground of Rejection

The fifth ground of rejection presented for review is whether claim 42 was properly rejected under 35 U.S.C. 103(a) over Lefesvre et al. in view of Winkel, Adrion et al., Zanin et al., Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137), as applied to claims 33, 34, 36, 37, 38, 39, 40, and 43, and further in view of Tomoyasu (Applied And Environmental Microbiology, Jan. 1998, p. 376-382) (Official Action page 13, first full paragraph).

This claim is allowable at least for depending from an allowable claim.

Arguments Concerning the Sixth Ground of Rejection

The sixth ground of rejection presented for review is whether claims 41 and 44-54 were properly rejected under 35 U.S.C. 103(a) over Lefesvre et al., Winkel, Adrion et al. Zanin et al., ad Cha et al., Tomoyasu, as applied to claims 33, 34, 36, 37, 38, 39, 40- 43, and further in view of Privitera et al. (US 4,826,760) and Barocci et al. (Transpl. Int., 1993, 6:29-33) (Official Action page 14, first full paragraph).

These claims are allowable at least for depending from an allowable claim.

Conclusion

The Appellant has demonstrated that the pending rejections are each improper. Thus, favorable reconsideration and reversal of the Examiner's rejections, by the Honorable Board of Patent Appeals and Interferences, are respectfully solicited.

Respectfully submitted,

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(viii) **Claims Appendix**

1-32. (cancelled)

33. (previously presented) A system for managing batches of immunocompetent cells collected from human or animal subjects for their deferred use, said system comprising for each of said human or animal subjects:

- a storage device for conditioning and preserving batches of immunocompetent cells successively collected, into one or more storage centers,

- a personal library processor for constituting from said collected batches a personal library of immunocompetent cells, said personal library cumulating a sum of immunity information stored in the membranes of collected immunocompetent cells,

- a collection device for collecting, during successive collections of batches, information that is characteristic of said human or animal subject's status of health and/or psychological status, before or during immunocompetent cells collection, said status characterizing information being obtained by processing measurements made on samples of blood and/or fluid and secretions and/or hair collected on said human or animal subject,

- a status-characterizing information device processing said status-characterizing information to determine said subject's identity data, said identity data including immunity-related data, historical and clinical data on previous diseases, treatments and therapeutic protocols experienced by said subject, said status-characterizing information device comprising an expert system wherein said status-characterizing information corresponding to said subject are entered in the form of biological items to which a set of rules stored in a knowledge base is applied, implementing into said expert system a process for determining a deferred-use protocol, said deferred-use protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells previously collected from said subject,

- a cell management database processor for storing said subject's identity data successively determined into a cell management database,

- an identification device for performing identification of the personal batches of cells and a consulting device for consulting said cell management database, and

- a processor for processing said successively collected subject's identity data to determine parameters of a deferred-use protocol for said identified batches of immunocompetent cells, said processor configured for upon prescription of a re-use process of immunocompetent cells for said subject:

- determining parameters of said deferred-use protocol, using data stored in said database, said determined parameters including optimized proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, using the subject's immunity data stored in said database, and

- determining said selected immunocompetent cells for extraction from said personal cell library.

34. (previously presented) The system according to claim 33, further comprising a bio-electronic device for collecting bio-electronic information.

35. (cancelled)

36. (previously presented) A method for managing batches of immunocompetent cells collected from human or

animal subjects for deferred use, comprising for each of said human subjects:

plural successive cell collections stages of collecting immunocompetent cells collected from a human or animal subject for deferred use;

storing the collected cells, in a storage device for conditioning and preserving the collected cells, into one or more storage centers;

constituting for said subject, a personal cell library from the successively collected cells and a personal database, stored within a physical medium accessible by a computer system, containing:

data resulting from successive status characterization stages effected before or during each cell collection stage, said data comprising information on said subject's physiologic identity and state of health, and

subject's identity data generated by use of an expert system executed within the computer system and wherein said status-characterizing information corresponding to said subject are entered in the form of biological items to which a set of rules stored in a knowledge base is applied,

implementing into said expert system a process for determining a deferred-use protocol, said deferred-use

protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells previously collected from said subject,

upon prescription of a re-use process of immunocompetent cells for said subject:

- determining parameters of said deferred-use protocol, using data stored in said database, said determined parameters including optimal proportions of various selected types of cells among cells stored in said personal cell library for better tolerance by said patient and a greater reaction speed, using subject's immunity data stored in said database,

- extracting said selected immunocompetent cells from said personal cell library, and

- processing said extracted immunocompetent cells according to said deferred-use protocol, in view or re-using said processed cells into said subject.

37. (previously presented) The method according to claim 36, comprising the further step of:

plural successive status-characterization stages of collecting information characteristic of the status of health and/or the psychological status of said subject, said

status-characterizing information being obtained by processing measurements made on samples selected from a group consisting of blood, fluid, secretions, hair and combinations thereof from said subject, said status-characterizing information yielding a subject status characterization result indicating the status of health status and/or the psychological status of said subject, and said collecting step further including

i) conditioning and preserving said collected cells in batches of immunocompetent cells, said batches being stored into one or more storage centers, and

ii) constituting from said collected cells, a personal cell library of immunocompetent cells, said personal cell library containing a sum of immunity information stored in the membranes of the collected immunocompetent cells from one or more of said batches of immunocompetent cells.

38. (previously presented) The method according to claim 37, further comprising implementing said method in a gene therapy protocol.

39. (previously presented) The method according to claim 37, further comprising cryo-preserving a batch of immunocompetent cells.

40. (previously presented) The method according to claim 37, wherein the status-characterizing information comprise bioelectronic information resulting from processing respective measures of pH, oxidation-reduction potential Rh2 and resistivity ρ of blood previously collected on said human or animal subject,

41. (previously presented) The method according to claim 37, further comprising a step for checking annihilating antibodies in the batches of immunocompetent cells before any re-use of a batch.

42. (previously presented) The method according to claim 37, further comprising during conditioning a batch of immunocompetent cells previously collected, a step for immunomagnetically selecting purified lymphocytes or monocytes.

43. (previously presented) The method according to claim 37, wherein said database is located within a

management center controlling said one or more storage centers.

44. (previously presented) The method according to claim 36 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

45. (previously presented) The method according to claim 44, wherein the autologous vaccine is a vaccine for flu with cytotoxic activity.

46. (previously presented) The method according to claim 44, wherein the autologous vaccine is a vaccine to be injected in the lymphatic system of a subject.

47. (previously presented) The method according to claim 46, comprising a further step for checking antibodies in the batches of immunocompetent cells prior to injection and annihilating those that would harm the receiver.

48. (previously presented) The method according to claim 37 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

49. (previously presented) The method according to claim 38 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

50. (previously presented) The method according to claim 39 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

51. (previously presented) The method according to claim 40 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

52. (previously presented) The method according to claim 41 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

53. (previously presented) The method according to claim 42 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

54. (previously presented) The method according to claim 43 further comprising preparing an autologous vaccine using specific parameters of T4/T8 ratio.

(ix) **Evidence Appendix**

Declaration of Professor Dominique CHARRON provided in the Amendment filed May 12, 2011.

(x) **Related Proceedings Appendix**

None.